UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,647	11/27/2001	Bernd Riedl	BAYER 18A	1010

23599 7590 04/25/2008

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
04/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/993,647	RIEDL ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74,81,87,93,99-104,106-115 and 117-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74,81,87,93,99-104,106-115 and 117-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 74, 81, 87, 93, 99-104, 106-115 and 117-119 are pending in this application.

The following rejections are maintained:

1. Claims 74, 81, 87, 93, 99-103, 106-114 and 117 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the treatment of carcinoma of the colon (based on the *in vitro* treatment of the tumor cell lines HCT116 and DLD-1 provided in the specification), does not reasonably provide enablement for a method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas; or a method for inhibiting RAF-kinase in a human or mammal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons provided in the previous office action(s) are incorporated here by reference.

Applicant's arguments have been fully considered but they were not found to be persuasive. Applicant relies on the state of the art references, Kolch and Monia and argues that 'the references teach correlation of raf inhibition with the inhibition of the growth of a variety of tumor types'. Contrary to applicant's arguments, the state of the art references Kolch and/or Monia do not establish a therapeutic method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas generally. As explained in the previous office action, the state of the art is not indicative of the fact that treatments of all types of diseases encompassed by the instant claims are conventional or well known. The cited references are too speculative and invite further research into treatment of cancer diseases. For example, Monia at

page 668 provides that "the emergence of novel therapies that specifically reverse the oncogenic effect of these gene products has generally been slow". All references provided as evidence of enabling disclosure present no evidence that the claimed compounds actually have activity in treating all types of solid tumor, carcinoma, myeloid disorders or adenoma. There is no evidence of record that the claimed compounds are actually efficacious in treating all types of solid tumor, carcinoma, myeloid disorders or adenoma; or inhibit RAF-kinase generally.

Applicant's arguments based on the state of the art references – Monia, Kolch, Daum, WO 98/22103, etc. have been fully considered but not deemed to be persuasive. However, the cited references do not cure the deficiencies of the specification. Considered separately or together, these references invite further research into the treatment of solid tumor, carcinoma, myeloid disorder, adenoma, etc. through inhibition of RAF-kinase.

Applicant argues that 'Given the extent of the disclosure provided, it would at most involve routine experimentation for one of ordinary skill in the art to treat any of the other cancers with the named compounds'. The guidance in the specification is limited to an *in vitro* cell proliferation assay showing inhibition of two colon cancer cell lines; and summary instructions relating to an in vivo assay in mice that can be performed to determine the inhibition of a human adenocarcinoma cell line (see pages 94-96). There is no evidence of record how the provided data is directly involved in the pathogenesis of all types of solid tumors, carcinoma, myeloid disorders or adenoma and/or that simply inhibiting RAF-kinase will lead to treatment of all of these diseases. It is not routine for one skilled in the art to synthesize, purify, screen for RAF-kinase inhibition, and test for anticancer activity of the claimed compounds.

Applicant argues that 'claim 117 is drawn to a method of inhibiting raf-kinase in a human or other mammal and examiner has not identified any element of the claim for which the disclosure is deficient'. Claim 117 is directed towards 'a method for inhibiting RAF-kinase in a **human** or **mammal**' – which involves administering of the compound to human or mammal and therefore reaches through to the treatment of all types of diseases associated with RAF-kinase. The findings and conclusions in the cited publications are with respect to inhibition of RAF kinase and the application of such activity for specific types of cancerous growth. The development of the most efficacious strategy for the treatment of cancers is based on understanding the underlying mechanisms of carcinogenesis. This includes the knowledge that the carcinogenic process is a multi-step, multi-mechanism process and that no two cancers are alike, in spite of some apparent universal characteristics, such as their inability to have growth control, to terminally differentiate, to apoptose abnormally and to have an apparent extended or immortalized life span. Since tumor promotion phase involves multiple mechanisms, there is no existence of a single therapeutic approach. The evidence of record does not disclose any known compounds of similar structure, which have been demonstrated to inhibit RAF-kinase generally and thereby treat all diseases mediated by raf kinase; or treat all types of solid tumors, carcinomas, myeloid disorders or adenomas, when the compounds are administered to a human or a mammal.

2. Claims 74, 81, 87, 93, 99-104, 106-115 and 117-119 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over

claims 38, 89-91, 121 of copending Application No. 10/042,226. It is acknowledged that 'applicants will address the rejection when the instant claims are otherwise allowable'.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Deepak Rao/
Primary Examiner
Art Unit 1624

April 24, 2008